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Group Art Unit Unknown

HA

In re

Patent Application of

Phillip Wilson Howard

Application No. 10/598,470

Confirmation No.: 5823

Filed: August 31, 2006

Examiner: Unknown

"PYRROLOBENZODIAZEPINES"

INFORMATION DISCLOSURE STATEMENT  
PURSUANT TO 37 C.F.R. § 1.97(b)

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

The Examiner's attention is directed to the references which are listed on the attached Form PTO/SB/08B; copies of non-U.S. patent references are attached.

Citation of these references is respectfully requested.

No concession is made that these documents are prior art, and Applicant expressly reserves the right to antedate the documents as may be appropriate.

Respectfully submitted,

Charlene L. Yager  
Reg. No. 48,887

File No. 065435-9079 US00  
Michael Best & Friedrich LLP  
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Substitute for form 1449B/PTO

JAN, 16 2007

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(use as many sheets as necessary)

## Complete if Known

Application Number	10/598470
Filing Date	August 31, 2006
First Named Inventor	Phillip Wilson Howard
Group Art Unit	Unknown
Examiner Name	Unknown
Attorney Docket Number	065435-9079 US00

Sheet

1

of

12

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/BK/		ADAMS et al., "Molecular modelling of a sequence-specific DNA-binding agent based on the pyrrolo[2,1-c][1,4]benzodiazepines," <i>Pharm. Pharmacol. Commun.</i> (1999) 5:555-560
		ARIMA et al., "Studies on Tomaymycin, a New Antibiotic. I. Isolation and Properties of Tomaymycin," <i>J. Antibiotics</i> (1972) 25:437-444
		BAIRD, E.E. et al., "Solid phase synthesis of polyamides containing imidazole and pyrrole amino acids," <i>J. Am. Chem. Soc.</i> (1996) 118(26):6141-6146
		BANDO, T. et al., "Highly efficient sequence-specific DNA interstrand cross-linking by pyrrole/imidazole CPI conjugates," <i>J. Amer. Chem. Soc.</i> (2003) 125:3471-3485
		BARALDI, P.G. et al., "Design, synthesis and biological activity of a pyrrolo[2,1-c][1,4]benzodiazepine (PBD)-distamycin hybrid," <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , vol. 8, No. 21, 3019-3024 (1998)
		BARALDI, P.G. et al., "Synthesis, in Vitro Antiproliferative Activity, and DNA-Binding Properties of Hybrid Molecules Containing Pyrrolo[2,1-c][1,4]benzodiazepine and Minor-Groove-Binding Oligopyrrole Carriers," <i>J. Med. Chem.</i> , 42, 5131-5141 (1999)
		BARALDI, P.G. et al., "[2,1-c][1,4]benzodiazepine (PBD)-distamycin hybrid inhibits DNA binding to transcription factor Sp1," <i>Nucleotides and Nucleic Acids</i> (2000) 19(8):1219-1229
		BARKER, P. et al., "2-(Trichloroacetyl)pyrroles as intermediates in the preparation of 2,4-disubstituted pyrroles," <i>J. Org. Chem.</i> (1978) 43:4849-4853
↓		BERGE et al., "Pharmaceutical Salts," <i>J. Pharm. Sci.</i> (1977) 66:1-19

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Sheet	2	of	12	Attorney Docket Number	065435-9079 US00

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/BK/	BERRY, J. M. et al., "Solid-phase synthesis of DNA-interactive pyrrolo[2,1-c][1,4]benzodiazepines," <i>Tetrahedron Letters</i> (2000) 41:6171-6174				
	BOGER et al., "CC-1065 and the Duocarmycins: Synthetic Studies," <i>Chem. Rev.</i> (1997) 97:787-828				
	BOGER, D.L. et al., "Total synthesis of distamycin A and 2640 analogues: a solution-phase combinatorial approach to the discovery of new, bioactive DNA binding agents and development of a rapid, high-throughput screen for determining relative DNA binding affinity or DNA binding sequence selectivity," <i>J. Am. Chem. Soc.</i> (2000) 122:6382-6394				
	BOGER, D.L. et al., "CBI-TMI: Synthesis and evaluation of a key analog of the duocarmycins. Validation of a direct relationship between chemical solvolytic stability and cytotoxic potency and confirmation of the structural features responsible for the distinguishing behavior of enantiomeric pairs of agents," <i>J. Am. Chem. Soc.</i> (1994) 116:7996-8006				
	BOGER, D.L. et al., "Synthesis of N-(tert-Butyloxycarbonyl)-CBI, CBI, CBI-CDPI, and CBI-CDPI: Enhanced functional analogues of CC-1065 incorporating the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) left-hand subunit," <i>J. Org. Chem.</i> (1990) 55(23):5823-5832				
	BOGER, D.L. et al., "Total synthesis and evaluation of (±)-N-(tert-Butyloxycarbonyl)-CBI, (±)-CBI-CDPI, and (±)-CBI-CDPI2: CC-1065 functional agents incorporating the equivalent 1,2,9,9a-tetrahydrocycloprop[1,2-c]benz[1,2-e]indol-4-one (CBI) left-hand subunit," <i>J. Am. Chem. Soc.</i> (1989) 111(16):6461-6463				
	BORGATTI, M. et al., "Inhibition of NF-κB/DNA interactions and HIV-1 LTR directed transcription by hybrid molecules containing pyrrolo [2,1-c][1,4] benzodiazepine (PBD) and oligopyrrole carriers," <i>Drug Development Research</i> (2003) 60(3):173-185				
	BOSE et al., "New Approaches to Pyrrolo[2,1-c][1,4]benzodiazepines: Synthesis, DNA-binding and cytotoxicity of DC-81," <i>Tetrahedron</i> , 48, 751-758 (1992)				
↓	BOSE, D.S. et al., "Rational Design of a Highly Efficient Irreversible DNA Interstrand Cross-Linking Agent Based on the Pyrrolobenzodiazepine Ring System," <i>J. Am. Chem. Soc.</i> , 114, 4939-4941 (1992)				

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	BRIEHN, C.A. et al., "Alternative heterocycles for DNA recognition: the benzimidazole/imidazole pair," <i>Chem. Eur. J.</i> (2003) 9:2110-2122
	CHEN, Z. et al., "A novel approach to the synthesis of cytotoxic C2-C3 unsaturated pyrrolo[2,1-c][1,4]benzodiazepines (PBDs) with conjugated acrylic C2-substituents," <i>Biorg. Med. Chem. Lett.</i> (2004) 14:1547-1549
	COOPER, N. et al., "Synthesis of novel PBDs as anti-tumour agents," <i>Chem. Commun.</i> (2002) 16:1764-1765
	COURTNEY, S. M. et al., "A new convenient procedure for the synthesis of pyrrolo[2,1-c][1,4]benzodiazepines", <i>Tetrahedron Letters</i> , vol. 34, No. 33, 5327-28 (1993)
	DAMAYANTHI, Y., et al., "Design and synthesis of novel pyrrolo{2,1-c}[1,4] benzodiazepine-Lexitropsin Conjugates," <i>J. Org. Chem.</i> , 64, 290-292 (1999)
	DROST, K.J. and CAVA, M.P., "A Photochemically Based Synthesis of the Benzannelated Analogue of the CC-1065 A Unit," <i>J. Org. Chem.</i> , 56:2240-2244 (1991)
	FARMER, J.D. et al., "DNA binding properties of a new class of linked anthramycin analogs," <i>Chemical Abstracts</i> , Abstract No. 239940r, vol. 114, No. 25, 25 899-903 (1991)
↓	FOLOPPE, M.P. et al., "DNA-binding properties of pyrrolo[2,1-c][1,4]benzodiazepine N10-C11 amidines," <i>Eur. J. Med. Chem.</i> , 31, 407-410 (1996)

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/BK/	FUJISAWA PHARMACEUTICAL CO., LTD., Abstract No. 139983k, "Benzodiazepine derivatives", <i>Chemical Abstracts</i> , vol. 99, No. 17, 603 (1983)
	FUJISAWA PHARMACEUTICAL CO., LTD., Abstract No. 72145x, "Benzodiazepine derivatives", <i>Chemical Abstracts</i> , vol. 98, No. 9, 638 (1983)
	FUJISAWA PHARMACEUTICAL CO. LTD., "Benzodiazepine derivatives," <i>SciFinder Scholar</i> , 2-3 (2002)
	FUKUYAMA, T. et al., "Total Synthesis of (+)-Porothramycin B," <i>Tetrahedron Letters</i> , vol. 34, 16, 2577-2580 (1993)
	FUKUYAMA, T. et al., "Facile reduction of ethyl thiol to aldehydes: application to a total synthesis of (+)-neothramycin a methyl ether," <i>J. Am. Chem. Soc.</i> (1993) 7050-7051
	GREENE, T.W. and WUTS, P.G.M., <i>Protective Groups in Organic Synthesis</i> , John Wiley & Sons, 2 <sup>nd</sup> ed., Ch 7, 315-345 (1991)
	GREGSON, S. et al., "Synthesis of a novel C2/C2'-exo unsaturated pyrrolobenzodiazepine cross-linking agent with remarkable DNA binding affinity and cytotoxicity," <i>Chemical Communications</i> , 797-798 (1999)
	GREGSON, S.J. et al., "Effect of C2/C3-endo unsaturation on the cytotoxicity and DNA-binding reactivity of pyrrolo-[2,1-c][1,4]-benzodiazepines," <i>Bioorg. Med. Chem. Lett.</i> (2000) 10(16):1849-1851
↓	GREGSON, S.J. et al., "Design, Synthesis and Evaluation of a Novel Pyrrolobenzodiazepine DNA-Interactive Agent with Highly Efficient Cross-Linking Ability and Potent Cytotoxicity", <i>J. Med. Chem.</i> , 44: 737-748 (2001)

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	GREGSON, S.J. et al., "Linker length modulates DNA cross-linking reactivity and cytotoxic potency of C8/C8' ether-linked C2-exo-unsaturated pyrrolo[2,1-c][1,4]benzodiazepine (PBD) dimers," <i>J. Med. Chem.</i> (2004) 1161-1174
	GREGSON, S.J. et al., "Synthesis of the first example of a C2-C3/C2'-C3'-endo unsaturated pyrrolo[2,1-c][1,4]benzodiazepine dimer," <i>Biorg. Med. Chem. Lett.</i> (2001) 11:2859-2862
	GREGSON, S.J. et al., "Synthesis of the first examples of A-C8/C-C2 amide-linked pyrrolo[2,1-c][1,4]benzodiazepine dimers," <i>Biorg. Med. Chem. Lett.</i> (2003) 13:2277-2280
	GREHN, L. et al., "Synthesis and antiviral activity of distamycin A analogues: substitutions on different pyrrole nitrogens and in the amidine function," <i>J. Med. Chem.</i> (1983) 26:1042-1049
	GUIOTTO, A. et al., "Synthesis of novel C7-aryl substituted pyrrolo[2,1-c][1,4]benzodiazepines (PBDs) via Pro-N10-troc protection and suzuki coupling," <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , 8, No. 21, 3017-3018 (1998)
	HARA et al., "DC 102, a new glycosidic pyrrolo(1,4)benzodiazepine antibiotic produced by <i>streptomyces</i> sp.", <i>J. Antibiotics</i> , 41, 702-704 (1988)
	HARTLEY, J.A. et al., "An agarose gel method for the determination of DNA interstrand crosslinking applicable to the measurement of the rate of total and 'second arm' crosslink reactions," <i>Anal. Biochem.</i> (1991) 193:131-134
↓	HOCHLOWSKI, J. et al., "Abbeymycin, a new anthramycin-type antibiotic produced by a streptomycete," <i>J. Antibiotics</i> , 40, 145-148 (1987)

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/BK/	HURLEY, L. and NEEDHAM-VANDEVANTER, D., "Covalent Binding of Antitumor Antibiotics in the Minor Groove of DNA. Mechanism of Action of CC-1065 and the Pyrrolo(1,4)benzodiazepines," <i>Acc. Chem. Res.</i> , 19, 230-237 (1986)
	ITOH et al., "Sibanomicin, a new pyrrolo(1,4)benzodiazepine antitumor antibiotic produced by a <i>micromonospora</i> sp." <i>J. Antibiotics</i> , 41, 1281-1284 (1988)
	KAMAL, A., et al., "An Efficient Synthesis of Pyrrolo[2,1-c][1,4] Benzodiazepine Antibiotics via Reductive Cyclization," <i>Bioorg. Med. Chem. Ltrs</i> , 7, No. 14, 1825-1828 (1997)
	KAMAL, A., et al., "Synthesis of Pyrrolo [2,1-c][1,4]-Benzodiazepene Antibiotics: Oxidation of Cyclic Secondary Amine with TPAP", <i>Tetrahedron</i> , v. 53, No. 9, 3223-3230 (1997)
	KAMAL et al., "Synthesis and DNA-binding affinity of A-C8/C-C2 alkoxyamido-linked pyrrolo[2,1-c][1,4]benzodiazepine dimers" <i>Biorg. Med. Chem. Lett.</i> (2003) 13(22):3955-3958
	KAMAL, et al., "Synthesis of pyrrolo[2,1-c][1,4]benzodiazepines via reductive cyclization of w-azido carbonyl compounds by TMSI: an efficient preparation of antibiotic DC-81 and its dimers," <i>Biorg. Med. Chem. Lett.</i> (2000) 10:2311-2313
	KANEKO, T. et al., "Bicyclic and tricyclic analogues of anthramycin," <i>J. Med. Chem.</i> (1985) 28:388-392
	KANG, G.-D. et al., "Synthesis of a novel C2-aryl substituted 1,2-unsaturated pyrrolobenzodiazepine," <i>Chem. Commun.</i> (2003) 1688-1689
↓	KOHN, K., "Anthramycin," <i>Antibiotics III</i> , Springer-Verlag, NY, 3-11 (1975)

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	KUMAR, R. et al., "Synthesis and antitumor cytotoxicity evaluation of novel pyrrolo[2,1-c][1,4]benzodiazepine imidazole containing polyamide conjugates," <i>Oncology Research</i> (2003) 13(4):221-233		
	KUMAR, R. et al., "Design and synthesis of novel pyrrolo[2,1-c][1,4]benzodiazepine - imidazole containing polyamide conjugates," <i>Heterocyclic Communications</i> (2002) 81(1):19-26		
	KUMAR, R. et al., "Design, synthesis and <i>in vitro</i> cytotoxicity studies of novel pyrrolo [2,1][1,4]benzodiazepine-glycosylated pyrrole and imidazole polyamide conjugates," <i>Org. Biomol. Chem.</i> (2003) 1(19):3327-3342		
	KUNIMOTO et al., "Mazethramycin, a new member of anthramycin group antibiotics," <i>J. Antibiotics</i> , 33, 665-667 (1980)		
	LANGLEY, D.R. and THURSTON, D.E., "A versatile and efficient synthesis of carbinalamine-containing pyrrolo[1,4]benzodiazepines via the cyclization of N-(92-aminobenzoyl)pyrrolidine-2-carboxaldehyde diethyl thioacetals: total synthesis of prothracarcin," <i>J. Org. Chem.</i> , 52, 91-97 (1987)		
	LANGLOIS, N. et al., "Synthesis and cytotoxicity on sensitive and doxorubicin-resistant cell lines of new pyrrolo[2,1-c][1,4]benzodiazepines related to anthramycin," <i>J. Med. Chem.</i> (2001) 44:3754-3757		
	LEBER, J.D. et al., "A revised structure for sibiromycin," <i>J. Am. Chem. Soc.</i> , 110, 2992-2993 (1988)		
↓	LEIMGRUBER, W. et al., "Isolation and characterization of anthramycin, a new antitumor antibiotic," <i>J. Am. Chem. Soc.</i> , 87, 5791-5793 (1965)		

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/BK/	LEIMGRUBER, W. et al., "The structure of anthramycin," <i>J. Am. Chem. Soc.</i> , 87, 5793-5795 (1965)
	LEIMGRUBER, W. et al., "Total synthesis of anthramycin," <i>J. Am. Chem. Soc.</i> , 90, 5641-5643 (1968)
	LESCRINIER, T. et al., "DNA-Binding Ligands from Peptide Libraries Containing Unnatural Amino Acids," <i>Chem. Eur. J.</i> , 4, 3, 425-433 (1998)
	LOWN et al., "Molecular Mechanism of Binding of Pyrrolo(1,4)benzodiazepine antitumour agents to deoxyribonucleic acid - anthramycin and tomaymycin," <i>Biochem. Pharmacol.</i> (1979), 28 (13), 2017-2026
	MISCHIATI, C. et al., "Binding of hybrid molecules containing pyrrolo [2,1-c][1,4]benzodiazepine (PBD) and oligopyrrole carriers to the human immunodeficiency type 1 virus TAR-RNA," <i>Biochem. Pharmacol.</i> (2004) 67(3):401-410
	MONKS, A. et al., "Feasibility of High-Flux Anticancer Drug Screen Using a Diverse Panel of Cultured Human Tumor Cell Lines," <i>Journal of National Cancer Institute</i> , 83, 757-766 (1991)
	MORI, M. et al., "Total syntheses of prothracarcin and tomaymycin by use of palladium catalyzed carbonylation," <i>Tetrahedron</i> (1986) 42(14):3793-3806
	MOUNTZOURIS, J.A. et al., "Comparison of a DSB-120 DNA interstrand cross-linked adduct with the corresponding bis-Tomaymycin adduct," <i>J. Med. Chem.</i> (1994) 37:3132-3140
↓	NAGASAKA, T. and KOSEKI, Y, "Stereoselective Synthesis of Tilivalline," <i>Journal of Organic Chemistry</i> , vol. 63, No. 20, 6797-6801 (1998)

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Sheet	9	of	12	Filing Date	August 31, 2006
				First Named Inventor	Phillip Wilson Howard
				Group Art Unit	Unknown
				Examiner Name	Unknown
				Attorney Docket Number	065435-9079 US00

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/BK/	NAGASAKA, T. et al., "Stereoselective Synthesis of Tilivalline," <i>Tetrahedron Letters</i> , 30:14, 1871-1872 (1989)
	O'NEIL, I.A., et al., "The Synthesis of Functionalized Pyrrolo-[2,1-c][1,4]-Benzodiazepines," <i>Synlett</i> , 75-78 (1997)
	O'NEIL, Chemical Abstract No. 171573p, "The synthesis of Functionalized Pyrrolo-[2,1-c][1,4]-Benzodiazepines", <i>Chemical Abstracts</i> , vol. 126, No. 13, 618 (1997)
	O'NEIL, I.A. et al., "DPPE: A Convenient Replacement for Triphenylphosphine in the Staudinger and Mitsunobu Reactions", <i>Tetrahedron Letters</i> , vol. 39, No. 42, 7787-7790 (1998)
	RAWAL, V.H. et al., "Photocyclization Strategy for the Synthesis of Antitumor Agent CC-1065: Synthesis of Dideoxy PDE-I and PDE-II. Synthesis of Thiophene and Furan Analogues of Dideoxy PDE-I and PDE-II," <i>J. Org. Chem.</i> , 52, 19-28 (1987)
	REDDY et al., "Design, synthesis and in vitro cytotoxicity studies of novel pyrrolo[2,1-c][1,4]benzodiazepine (PBD)-polyamide conjugates and 2,2'-PBD dimers," <i>Anti-Cancer Drug Design</i> (2000) 15(3):225-238
	REDDY, B.S. Praveen et al., "Synthetic DNA minor groove-binding drugs," <i>Pharm. Thera.</i> (1999) 84:1-111
	RENNEBERG, D. et al., "Imidazopyridine/pyrrole and hydroxybenzimidazole/pyrrole pairs for DNA minor groove recognition," <i>J. Am. Chem. Soc.</i> (2003) 125:5707-5716
↓	REYNOLDS, V.L. et al., "The chemistry, mechanism of action and biological properties of CC-1065, a potent antitumor antibiotic," <i>J. Antibiotics</i> (1986) 39(3):319-334

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/BK/	SAGNOU, M.J. et al., "Design and Synthesis of Novel Pyrrolobenzodiazepine (PDB) Prodrugs for ADEPT and GDEPT," <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , 10, 2083-2086 (2000)		
	SHIMIZU, K et al., "Prothracarcin, a Novel Antitumor Antibiotic," <i>J. Antibiotics</i> , 35, 972-978 (1982)		
	SMELLIE, M. et al., "Cellular pharmacology of novel C8-linked anthramycin-based sequence-selective DNA minor groove cross-linking agents," <i>Br. J. Cancer</i> (1994) 70:48-53		
	SMELLIE, M. et al., "Sequence selective recognition of duplex DNA through covalent interstrand cross-linking," <i>Biochem.</i> (2003) 42:8232-8239		
	SUGGS, J.W. et al., "Synthesis and structure of anthramycin analogs via hydride reduction of dilactams," <i>Tetrahedron Letters</i> , 26, No. 40, 4871-4874 (1985)		
	TAKEUCHI, T. et al., "Neothramycins A and B, New Antitumor Antibiotics," <i>J. Antibiotics</i> , 29, 93-96 (1976)		
	TERCEL, M. et al., "Unsymmetrical DNA cross-linking agents: combination of the CBI and PBD pharmacophores," <i>J. Med. Chem.</i> (2003) 46:2132-2151		
	THURSTON, D.E. and THOMPSON, A.S., "The molecular recognition of DNA," <i>Chem. Brit.</i> , 26, 767-772 (1990)		
↓	THURSTON, D.E. and BOSE, D.S., "Synthesis of DNA-Interactive Pyrrolo[2,1-c][1,4]benzodiazepines," <i>Chem. Rev.</i> , 94:433-465 (1994)		

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/BK/	THURSTON, D. E., "Advances in the study of Pyrrolo[2,1-c][1,4] benzodiazepine (PBD) Antitumour Antibiotics", <i>Molecular Aspects of Anticancer Drug-DNA Interaction</i> , Neidle, S. and Waring, M.J., Eds.; Macmillan Press Ltd, 1:54-88 (1993)		
	THURSTON, D.E. et al., "Effect of A-ring modifications on the DNA-binding behavior and cytotoxicity of pyrrolo[2,1-c][1,4]benzodiazepines", <i>Journal of Medicinal Chemistry</i> , 42:1951-1964 (1999)		
	THURSTON, D.E. et al., "Synthesis of Sequence-selective C8-linked Pyrrolo [2,1-c][1,4] Benzodiazepine DNA Interstrand Cross-linking Agent," <i>J. Org. Chem.</i> , 61:8141-8147 (1996)		
	THURSTON, D.E. et al., "Synthesis of a novel GC-specific covalent-binding DNA affinity-cleavage agent based on pyrrolobenzodiazepines (PBDs)," <i>Chemical Communications</i> , 563-565 (1996)		
	THURSTON, D.E., "Nucleic acid targeting: therapeutic strategies for the 21st century," <i>Brit. J. Cancer</i> (1999) 80(1):65-85		
	TIBERGHIEN, A.C. et al., "Application of the stille coupling reaction to the synthesis of C2-substituted endo-exo unsaturated pyrrolo[2,1-c][1,4]benzodiazepines (PBDs)," <i>Biorg. Med. Chem. Lett.</i> (2004) 14:5041-5044		
	TSUNAKAWA, M. et al., "Porothramycin, a new antibiotic of the anthramycin group: Production, isolation, structure and biological activity," <i>J. Antibiotics</i> , 41:1366-1373 (1988)		
	UMEZAWA, H. et al., Chemical Abstract No. 4427a, "Mazethramycins" <i>Chemical Abstracts</i> , vol. 90, No. 1, 428 (1979)		
↓	UMEZAWA, H. et al., "Mazethramycins," <i>SciFinder Scholar</i> , 2-3 (2002)		

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/BK/	WELLS, G. et al., "Pyrrolobenzodiazepine-polyamide libraries: synthesis and DNA binding selectivity," <i>Proc. Am. Assoc. Canc. Res.</i> (2003) 44:85-86, #452
/BK/	WILSON, S.C. et al., "Design and Synthesis of a Novel Epoxide-Containing Pyrrolo[2,1-c][1,4]benzodiazepine (PBD) via a New Cyclization Procedure," <i>Tetrahedron Letters</i> , 36, No. 35, 6333-6336 (1995)
/BK/	WILSON, S.C. et al., "Design, Synthesis, and Evaluation of a Novel Sequence-Selective Epoxide-Containing DNA Cross-Linking Agent Based on the Pyrrolo[2,1-c][1,4]benzodiazepine System", <i>J. Med. Chem.</i> 42:4028-4041 (1999)

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